DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

January 31, 2016

Diazyme Laboratories
Abhijit Datta, Ph.D.
Director, Technical Operations
12889 Gregg Court
Poway, CA 92064

Re: K143470
Trade/Device Name: Diazyme Fibrinogen Assay
Diazyme Fibrinogen Calibrator Set
Diazyme Fibrinogen Control Set
Regulation Number: 21 CFR 864.7340
Regulation Name: Fibrinogen determination system
Regulatory Class: Class II
Product Code: GIS, GFX, GIL
Dated: January 15, 2016
Received: January 19, 2016

Dear Dr. Datta:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act

or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director
Division of Immunology and Hematology Devices
Office of *In Vitro* Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
K143470

Device Name
Diazyme Fibrinogen Assay; Diazyme Fibrinogen Calibrator Set; Diazyme Fibrinogen Control Set

Indications for Use *(Describe)*
The Diazyme Fibrinogen Assay is for the quantitative determination of fibrinogen levels in citrated human plasma. For in vitro diagnostic use only.

The Diazyme Fibrinogen Calibrator Set is intended for use in the calibration of the Diazyme Fibrinogen Assay. For in vitro diagnostic use only.

The Diazyme Fibrinogen Control Set is intended for use as quality controls for the Diazyme Fibrinogen Assay. For in vitro diagnostic use only.

The performance of this device has not been established in neonate and pediatric patient populations.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Submitter's name:	Diazyme Laboratories
Submitter's address:	12889 Gregg Court Poway, CA 92064 USA
Name of Contact Person:	Dr. Abhijit Datta Diazyme Laboratories 12889 Gregg Court Poway, CA 92064 Phone: 858-455-4762 Fax: 858-455-2120
Date the Summary was Prepared:	January 15, 2016
Name of the Device	Diazyme Fibrinogen Assay Diazyme Fibrinogen Calibrator Set Diazyme Fibrinogen Control Set
Trade Name:	Diazyme Fibrinogen Assay Diazyme Fibrinogen Calibrator Set Diazyme Fibrinogen Control Set
Common/Usual Name	Diazyme Fibrinogen Assay
Device Classification Name	Fibrinogen, Antigen, Antiserum, Control, Calibrator
Product code:	GIS, Fibrinogen Determination System GFX, Fibrinogen Standard GIL, Plasma, Fibrinogen Control
Panel:	Hematology
Submission Type	Traditional 510k
Regulation Number	21CFR 864.7340 Fibrinogen determination system
Device Class	Class II
Predicate Device:	Kamiya K-Assay Fibrinogen (k993482)
Manufacturing Address	Diazyme Laboratories

12889 Gregg Court
Poway, CA 92064
USA

Establishment Registration 2032900

DESCRIPTION OF THE DEVICE

Clinical Significance

Fibrinogen is a ~340 kDa plasma glycoprotein essential to blood clot formation. In the final step of the coagulation cascade, thrombin cleaves fibrinogen to form insoluble fibrin monomers, which then polymerize to form fibrin clots.

Abnormal plasma fibrinogen quality or quantity can occur as inherited or acquired disorders. Higher levels of fibrinogen are associated with inflammation, trauma, surgery, and pregnancy. A decrease of the fibrinogen level is observed in disseminated intravascular coagulation (DIC), fibrinolysis and hereditary diseases. Additionally, fibrinogen is an acute phase reactant, thus upregulated during inflammation or tissue damage.

Assay Principle

The Diazyme Fibrinogen Assay is based on an immunoturbidimetric assay. Fibrinogen in plasma binds to specific anti-fibrinogen antibody and forms immune complexes. The degree of turbidity caused by immune complexes can be measured optically at 340nm, and is proportional to the quantity of fibrinogen in the sample. The instrument calculates the fibrinogen concentration by interpolation of obtained signal of a 4-point calibration curve prepared from calibrators of known concentrations.

Detailed Device Description

Diazyme Fibrinogen Assay System consists of the following items:

1. The Diazyme Fibrinogen Assay: containing reagent R1 and reagent R2. Reagent 1 contains buffer, saline, and sodium azide. Reagent 2 containing anti-human fibrinogen Ig fraction tittered to optimal concentrations dependent on sera lot and sodium azide.

2. Diazyme Fibrinogen Calibrator Set: 3 levels, serum based, intended for use in the calibration of the Diazyme Fibrinogen Assay. The calibrators are in lyophilized form containing purified human fibrinogen antigen, defibrinated human serum and sodium azide

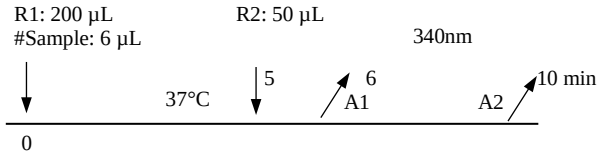
3. Diazyme Fibrinogen Control Set: 2 levels, serum based, intended for use as quality controls for the Diazyme Fibrinogen Assay. The controls are in lyophilized form containing purified human fibrinogen antigen, defibrinated human serum and sodium azide.

The Diazyme Fibrinogen Assay is run on Roche Modular P analyzer (K953239/005). The Diazyme Fibrinogen Assay never comes into direct contact with patients. The patient's venous

blood sample is first collected by a phlebotomist and then submitted for determination of fibrinogen concentration using Diazyme Fibrinogen Assay by trained professionals.

The Control Unit of the Roche Modular P analyzer uses a graphical interface to control all instrument functions. The computer, keyboard, and touchscreen monitor allows users to navigate through the software, enter assay, calibrator, and control information, and make test selections. The Diazyme Fibrinogen Modular P application parameters provided are programmed into the Modular P analyzers. The reagents, calibrators and controls are loaded into the analyzer. The Roche Modular P stores the Diazyme Fibrinogen Assay reagents in a refrigerated compartment. Reagent and sample pipettes automatically aspirate and dispense specified amounts of reagent or calibrators, controls, and sample into reaction cells. The change in absorbance is measured at specified wavelengths.

See Reaction Scheme.



After a 4-point calibration, spline-fitting is used to smoothly fit polynomial functions through mean values of the response for calibrators of known concentrations. The Roche Modular P calculates the fibrinogen concentration of a patient sample by interpolation of the obtained signal to a stored 4-point calibration curve.

#: The Modular P analyzer performs automatic on-board 1: 20 dilution using saline (5 µL + 100 µL saline).

Use the provided Diazyme Fibrinogen Assay (DZ768A) Application Parameters for Roche Modular P and enter the application parameters via the keyboard, settings sheet or barcode sheet, as appropriate.

Modular P Applications	
Measuring mode	Absorbance
Abs. calculation mode	2 Point END
Reaction mode	S-R1/R3
Reaction direction	Increase
Primary/Secondary Wavelength	340 nm/700nm
Calc. first/last	18/34
Unit mg/dL	
<u>Pipetting parameters</u>	
R1	200 µL
Sample	5 µL
Sample diluent (saline)	100 µL (1:20 dilution)
Diluted Sample	6 µL
R2	50 µL
Total volume	256 µL

Indications for Use:

The Diazyme Fibrinogen Assay is for the quantitative determination of fibrinogen levels in citrated human plasma. For *in vitro* diagnostic use only.

The Diazyme Fibrinogen Calibrator Set is intended for use in the calibration of the Diazyme Fibrinogen Assay. For *in vitro* diagnostic use only.

The Diazyme Fibrinogen Control Set is intended for use as quality controls for the Diazyme Fibrinogen Assay. For *in vitro* diagnostic use only.

Performance Characteristics of Subject Device

Precision

The precision of the Diazyme Fibrinogen Assay was evaluated according to CLSI EP5-A2 guideline. In the study, 6 citrated plasma samples including one sample close to the very low end of the AMR and one sample close to the very high end of the AMR were tested with three lots of reagents. The results are summarized in the following table:

Sample Repeatability (Three Reagent Lots Combined)

Sample	N	Mean mg/dL	Within-Run (SD, %CV)	Between-Run (SD, %CV)	Between-Lot (SD, %CV)	Between-Day (SD, %CV)	Total (SD, %CV)
Plasma 1	240	453.4	8.0, 2%	9.4, 2%	16.2, 4%	10.6, 2%	23.0, 5%
Plasma 2	240	333.4	5.8, 2%	5.2, 2%	10.7, 3%	7.4, 2%	15.1, 5%
Plasma 3	240	208.6	3.0, 1%	3.2, 2%	6.6, 3%	4.9, 2%	9.3, 5%
Plasma 4	240	107.3	1.6, 2%	1.7, 2%	3.6, 3%	2.8, 3%	5.2, 5%
Plasma 5	240	706.8	11.9, 2%	13.9, 2%	27.1, 4%	20.1, 3%	38.4, 5%
Plasma 6	240	823.9	16.3, 2%	12.7, 2%	30.3, 4%	22.3, 3%	42.9, 5%

Additionally, three lots of the calibrators were tested for precision using three lots of the reagents calibrated with master lot of the calibrators. The calibrators were tested 2 runs per day over 10 working days.

Calibrator Repeatability (Three Reagent Lots and Three Calibrator Lots Combined)

Calibrator	N	Mean	Within-Run (SD, %CV)	Between-Run (SD, %CV)	Between Lot (SD, %CV)	Between-Day (SD, %CV)	Total (SD, %CV)
Level 1	360	262	5.7,2%	0,0%	13.3,5%	12.1,5%	18.8,7%
Level 2	360	578	17.9,3%	0,0%	27.9,5%	22.5,4%	40.1,7%
Level 3	360	1130	21.2,2%	0,0%	44.9,4%	40.4,4%	64.0,6%

Two lots of serum based controls were tested in duplicates per run, 2 runs per day for 20 days using two lots of the reagents.

Control Repeatability (Two Reagent Lots and One Control Lot Combined)

Sample	Mean (N=160)	Within-Run		Between-Run		Between-Lot		Between-Day		Total	
		SD	%CV	SD	%CV	SD	CV%	SD	%CV	SD	%CV
Level 1	173.2	2.3	1	1.4	1	4.1	2	3.1	2	4.1	2
Level 2	607.5	8.2	1	6.5	1	15.1	3	11.1	2	15.2	3

Multi-site precision (reproducibility) study was performed at two external sites and Diazyme site on Modular P analyzer. In this study, the same sets of 6 citrated plasma samples as used. Six citrated plasma including one sample close to the very low end of the AMR and one sample close to the high end of the AMR were tested. The results of the within-run, between-run, between-day, between-site and total CV% are listed in the following tables

Reproducibility Data Analysis (Three Sites, Three Calibrator and Control Lots combined)

Sample	N	Mean mg/dL	With-in		Between run		Between day		Between Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Plasma 1	60	408.5	10.2	3%	8.8	2%	27.5	7%	29.9	7.3%	42.8	10 %
Plasma 2	60	303.1	6.2	2%	2.3	1%	21.1	7%	21.6	7.1%	30.9	10 %
Plasma 3	60	195.5	2.9	2%	1.8	1%	9.6	5%	9.9	5.1%	14.2	7%
Plasma 4	60	100.0	1.2	1%	1.1	1%	5.0	5%	5.1	5.1%	7.4	7%
Plasma 5	60	701.5	22.4	3%	23.8	3%	29.9	4%	43.9	6.2%	62.2	9%
Plasma 6	60	818.4	13.6	2%	7.7	1%	9.1	1%	18.0	2.2%	25.5	3%
Calibrator1	120	250.7	3.8	2%	6.0	2%	11.7	5%	13.6	5.4%	19.3	8%
Calibrator2	120	502.1	11.0	2%	10.9	2%	14.0	3%	20.8	4.1%	29.5	6%
Calibrator3	120	1077.3	17.1	2%	14.9	1%	47.0	4%	51.8	4.8%	73.5	7%
Control 1	120	179.4	3.2	2%	1.9	1%	6.1	3%	7.1	4.0%	10.0	6%
Control 2	120	609.6	13.2	2%	12.6	2%	16.4	3%	24.4	4.0%	34.6	6%

Linearity

The eleven levels linearity set was prepared by mixing a pooled fibrinogen spiked plasma sample containing 1000 mg/dL fibrinogen and saline at different proportions according to Clinical and Laboratory Standards Institute EP6-A. The results showed that Diazyme Fibrinogen Assay is linear up to 1032.8 mg/dL. Based on linearity data, method comparison data, and limit of quantitation (LOQ = 12.9 mg/dL) study, and reference interval study, and predicate AMR, the analytical measuring range (AMR) of Diazyme Fibrinogen assay is claimed to be 100-900 mg/dL.

Method Comparison

Human plasma samples were tested with the Diazyme Fibrinogen Assay and the obtained results were compared to the predicate method according to CLSI EP9-A2 guideline. A total of 176 samples tested across 3 clinical sites. All samples were tested in singlet with both methods. The results are summarized in the following table:

Parameter	Regular Regression	Deming regression
n	176	176
Slope	0.986	0.989
95% CI	0.975 – 0.997	0.978 – 0.999
Intercept	2.72	1.80
95% CI	-1.70 – 7.13	-2.68 – 6.22
Standard Error of Estimate	15.31	15.32
Correlation Coefficient(R)	0.9973	0.9973
Sample Range (Diazyme)	107.5 – 870.0	107.5 – 870.0

Interference

The following substances normally present in the plasma produced less than 10% deviation when tested at levels equal to the concentrations listed below, according to CLIA EP7-A "Interference Testing in Clinical Chemistry".

The following endogenous substances do not interfere with this assay at the levels tested (less than 10% bias).

Interferent	Concentration
Ascorbic Acid	176 mg/dL
Bilirubin	40 mg/dL
Bilirubin Conjugated	40 mg/dL
Hemoglobin	1000 mg/dL
Rheumatoid Factor	220 IU/ml
Triglycerides	1000 mg/dL

The common therapeutic substances of Acetylsalicyclic Acid, Na2-Cefoxitin, Ibuprofen, fibrin degradation product and coagulation inhibitors such as warfarin, dabigatran, hirudin, rivaroxaban, and argatroban, heparin showed no significant interference (< ± 10%) up to the concentrations summarized below.

Interferent	Concentration
Acetylsalicylic Acid	2.78 mM
Na2-Cefoxitin	1554 µM
Ibuprofen	2438 µM
Warfarin	65 µM
Dabigatran	3.7 µg/mL
Hirudin	25 µg/mL
Rivaroxaban	7.0 µg/mL
Argatroban	20.0 µg/mL
FDP	0.5 mg/mL
Unfractionated Heparin	3000 U/L
Low molecular weight Heparin	3000 U/L

Summary of the Performance Characteristics of the subject Device in Comparison of the Predicate Device

Kamiya K-Assay Fibrinogen (K993482)	Diazyme Fibrinogen Assay	Equivalency
Assay Range: 100 – 900 mg/dL Precision: CV% of 1.8 – 13.0% Accuracy (vs Incstar ITA): Correlation Coefficient (R^2) = 0.990 Slope = 0.967 *y*-intercept = 33.91	Linear Range: 100 – 900 mg/dL Precision: CV of less than 10% Accuracy (vs. Kamiya K-Assay): Correlation Coefficient (R^2) = 0.9946 Slope = 0.986 *y*-intercept = 2.72	Similar

Summary of Assay Kit Components Comparing to the predicate device

Kamiya K-Assay Fibrinogen (K993482)	Diazyme Fibrinogen Assay	Equivalency
Reagent 1: Buffer Reagent Tris(hydroxymethyl)aminomethane (100mM), ready to use Reagent 2: Antiserum Reagent Anti-human fibrinogen goat antiserum Calibrator: Lyophilized calibrator	Reagent 1 Phosphate buffered saline solution, ready to use Reagent 2 Goat anti-human Fibrinogen reagent, ready to use Calibrators Lyophilized calibrators prepared with serum, purified human Fibrinogen, and 0.09% sodium azide	Same
Calibrator Set	Calibrator Set	
1 x 1.0 mL Single-Level Calibrator	1 x 1.0 mL Calibrator 1 1 x 1.0 mL Calibrator 2 1 x 1.0 mL Calibrator 3	Different
Control Set (plasma based)	Control Set (serum based)	
5 x 1.0mL Control 1 5 x 1.0mL Control 2	1 x 1.0mL Control 1 1 x 1.0mL Control 2	Similar

Rationale for Considering the Device Substantially Equivalent to Devices Approved for Inter-State Commerce

Kamiya K-Assay was selected for method comparison with Diazyme Fibrinogen Assay. The reagents used for the Diazyme Fibrinogen Assay are similar to the predicate and used to develop the application for the Roche Modular P analyzer. The design, key materials, and chemical composition are similar between subject device and predicate device. The method comparison study between the subject and predicate using clinical patient samples showed excellent

correlation. The similarities and differences between the predicate reagent and the Diazyme Fibrinogen Assay are given in the table above. Detailed performance characteristics and comparison analysis are given in the filing and demonstrate substantial equivalence to predicate device.

The performance characteristics of the Diazyme Fibrinogen Assay are substantially similar to that of the approved predicate test. Performance data and risk analysis indicates that differences should not affect the safety and effectiveness of the Diazyme Fibrinogen Assay and offers users an *in vitro* diagnostic device system to measure fibrinogen in human plasma.

Conclusion

Detailed method comparison analysis (accuracy studies) presented in this 510k submission, together with linearity, precision and interference studies, demonstrates that the Diazyme Fibrinogen Assay performance is acceptable, safe and effective. There is no significant deviation between the results obtained by Diazyme Fibrinogen Assay and the legally marketed predicate device Kamiya K-Assay Fibrinogen (k993482) when testing clinical patient samples and is thus substantially similar.